ATTACHMENT

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A. EPA's SCIENTIFIC APPROACH

EPA's methodology for hazard identification of health effects is based on a total weight-of-evidence approach, which encompasses evidence on exposure, physical and chemical properties, and toxicology, including animal and human studies. Because environmental tobacco smoke (ETS) contains over 4,000 individual components, including over 40 known human and animal carcinogens, examining components individually would be prohibitive. Instead, ETS was evaluated as a complex mixture. Also, the analysis focused on the respiratory system since that provided the largest database.

The methodologies used for the assessment of lung cancer and noncancer respiratory effects in the EPA report differ. First, lung cancer is only seen in adults and is thought to represent the effect of long-term exposure. The noncancer respiratory effects examined are most apparent in children, and some of these are irritation effects associated with acute exposures. Second, for lung cancer less is known about mechanisms than is the case for some of the childhood respiratory effects, and this leads to differences in the development of the evidence. Third, because there were 30 studies on lung cancer and ETS, this database was analyzed several different ways before arriving at an overall conclusion. For the various childhood respiratory effects that were examined, there were fewer studies of any one effect, and analysis was more limited.

For all effects, studies examine home smoking patterns as a surrogate for ETS exposure. The exposure surrogate in the studies of lung cancer among nonsmokers is spousal smoking patterns. For childhood respiratory effects, parental smoking is the most common surrogate, although recent studies have also shown high correlations between body metabolites of ETS and pneumonia, bronchitis, asthma, and fluid in the middle ear.

There is nearly universal exposure to ETS, which often clouds the distinction between "exposed" and "unexposed" subjects and makes any potential effects difficult to observe. To try to eliminate the effect of some of these misclassified exposures, two methods are used. For hazard identification purposes, trend analysis and analyses comparing high exposure groups with controls are conducted. For population risk estimates, a model which adjusts for background (i.e., non-home) exposures is used.

A.1. Lung Cancer

The conclusion that ETS is a human lung carcinogen is based on the total weight of the available scientific evidence. This evidence includes:

- the strong exposure-response relationships for active smoking for all 4 major lung cancer types, with no evidence of an exposure threshold;
- the chemical similarity of mainstream smoke and ETS, both of which contain over 40 carcinogens;
- supporting evidence from animal bioassays and genotoxicity studies;
- evidence of ETS exposure and uptake by nonsmokers; and
- data from 30 epidemiology studies of ETS and lung cancer from 8 different countries.

The epidemiology studies attempt to estimate the relative risk of lung cancer from actual environmental levels of ETS. Such investigations are inherently difficult for a variety of reasons, not the least of which is the fact that virtually everyone is exposed to some level of ETS from a variety of different sources. Therefore, the studies try to compare risks in people with greater versus lesser exposures. All 30 epidemiology studies provide data on female never-smokers classified as "exposed" or "unexposed" on the basis of whether or not their husbands smoke. Although spousal smoking status is the best single measure of ETS exposure, it is a crude measure, and the studies are prone to exposure misclassification which decreases their ability to detect an increased risk if one exists. Furthermore, many of the studies are of small size and have a low statistical power to detect an increased risk. Despite these difficulties, which make it likely that most studies will not detect an effect if it exists, analysis of the studies reveals consistent evidence linking ETS and lung cancer.

In the EPA report, the epidemiologic data are analyzed a variety of different ways, and each analysis demonstrates an association between ETS and lung cancer. First, the studies were analyzed individually. Using the crude "exposed" versus "unexposed" measure, 24 of the 30 studies found an increased risk of lung cancer in the exposed group; nine of these were statistically significant. This proportion (9/30) of significant studies is highly unlikely to have occurred by chance (probability < one in 10 thousand). In addition, all 17 studies with data categorized by exposure level (i.e., amount of spousal smoking) found an increased risk of lung cancer in the highest exposure group, and 9 of the 17 were statistically significant (probability < one in 10 million), despite the fact that most had a small sample size. Examining only the highest exposure group helps to minimize exposure misclassification in the "exposed" group, since women whose spouses smoke a lot are more likely to be exposed to substantial amounts of ETS. Finally, 10 of the 14

studies with sufficient data for a trend test showed a statistically significant exposure-response relationship (probability < one in a billion), i.e., increasing risk of lung cancer with increasing ETS exposure.

The study data were also combined by country, using a statistical procedure called "meta-analysis" to pool the data. Combining datasets increases the ability to detect an effect, if one is present, and provides an objective means of including all studies, both with positive and non-positive results, in the analysis. This combined analysis also showed increased risks, consistent with the analyses of the individual studies.

A number of potential modifying factors, such as diet and occupation, were also examined, and it was determined that they could not account for the observed increased risks. Furthermore, the consistency of the results across numerous independent studies from different countries argues against the existance of any one factor other than exposure to ETS as an explanation for the observed results.

In summary, the total weight of the evidence is strongly supportive of a conclusion that ETS causes lung cancer in humans, and this conclusion was unanimously endorsed by EPA's Science Advisory Board.

The population risk estimate of approximately 3,000 lung cancer deaths per year in U.S. nonsmokers is based on the pooled relative risk estimate for the 11 U.S. epidemiology studies on ETS and lung cancer, with an adjustment for other sources of ETS exposure in addition to spousal smoking. The adjustment uses biological markers of ETS exposure to assess relative ETS exposure between nonsmokers, with and without spousal exposure. The estimate of 3,000 is consistant with estimates generated in an alternative analysis based on the Fontham et al. study. This NCI-funded multicenter study was the largest U.S. case-control study and is considered representative of the U.S. population. It was designed specifically to examine ETS and lung cancer and pays special attention to eliminating smoker misclassification bias. Furthermore, it is the only study which provided data on both relative risk and relative exposure.

The overall estimate of approximately 3,000 lung cancer deaths is a composite of estimates of 1,500 for female never-smokers, 500 for male never-smokers, and 1,000 for long-term former smokers of both sexes. (These estimated 1,000 ETS-attributable lung cancer deaths in long-term former smokers are in addition to any lung cancer deaths resulting from former smoking.) To extend the analyses of female never-smokers to male never-smokers and to long-term former smokers, the estimated relative risks were converted to excess risks, and these excess risks were assumed to apply to the male never-smokers and the

former smokers. This assumption may underestimate the risk in male never-smokers and long-term former smokers, since, for example, males are exposed to greater levels of background ETS. An alternate breakdown of the estimated 3,000 lung cancer deaths attributes 800 deaths to "spousal" (or home) exposure and 2,200 deaths to other sources of exposure, such as work and public places. EPA has relatively high confidence in these estimates, especially those for female never-smokers, since they are based on increased risks observed in humans exposed to ETS at actual environmental levels--there is no extrapolation from high to low dose and no extrapolation from animals to humans.

The epidemiology data on workplace exposure were not included in the report for several reasons. The database is much smaller than the database for females and spousal smoking, with only 10 of the 30 studies reporting data for workplace exposures, and only two reporting risk by levels of exposure. Furthermore, workplace exposures are much more variable over time, with study subjects and their coworkers typically changing jobs several times during a lifetime. Recall of coworkers' smoking habits is less reliable than that of spousal habits; similarly, workers may not be aware of ETS exposures occurring through workplace ventilation systems. The data on female never-smokers and spousal smoking provide the largest database for the purposes of analyzing comparable data, and spousal smoking is a major source of ETS exposure that is relatively stable over time. The inference can be made that if exposure to ETS at home can cause lung cancer, then exposure to comparable levels of ETS in other indoor environments can also cause lung cancer. The EPA report documents exposure studies showing that ETS levels in workplaces where smoking occurs are comparable to levels in homes where smoking occurs.

A.2. Noncancer Respiratory Disorders

The weight of evidence for the noncancer respiratory disorders includes mechanistic information on tobacco smoke's effects on the lung, as well as data from over 100 epidemiological studies. Both maternal smoking during pregnancy and postnatal exposure to ETS can predispose a child to a variety of respiratory effects that can themselves have long-term consequences. Maternal smoking during pregnancy can affect the developing lung, causing permanent changes in lung structure and function, e.g. decreased lung elasticity. Postnatal exposures to ETS may similarly affect lung development, as well as increase bronchial responsiveness and enhance the process of allergic sensitization of the lung. These changes may predispose children to acute lower respiratory tract infections early in life, and to asthma, lower levels of lung function, and chronic airflow limitation later in life.

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Epidemiology studies have consistently demonstrated increased risks of lower respiratory tract infections in young children whose parents smoke. In addition, epidemiology studies of children show that ETS exposure is causally associated with increased prevalence of fluid in the middle ear, symptoms of upper respiratory tract irritation (e.g., coughing and wheezing), and reductions in lung function. ETS exposure is also causally associated with additional episodes and increased severity of symptoms in children with asthma. Furthermore, the data are suggestive that ETS exposure can cause new cases of asthma in children who have not previously displayed symptoms; however, there were too few studies to make a conclusive determination. No conclusions could be drawn about upper respiratory tract infections (i.e., colds and sore throats) or middle ear infections in children. The epidemiology studies of noncancer respiratory disorders in nonsmoking adults generally relied on spousal smoking as a surrogate for ETS exposure, and also demonstrated significant effects, including coughing, phlegm production, chest discomfort, and reduced lung function.

Because of the widespread exposure to ETS and the high incidence rates for respiratory illnesses and disorders, even small increases in risk can result in substantial numbers of cases being attributable to ETS. For example, acute lower respiratory tract infections are one of the leading causes of morbidity and mortality during infancy and childhood, and the EPA report estimates that ETS exposure is responsible for 150,000 to 300,000 cases in children up to 18 months, resulting in 7,500 to 15,000 hospitalizations, each year. Fluid in the middle ear is another common affliction in young children and is the most common reason for hospitalization of young children for an operation. As a final example of the public health impacts of ETS exposure, the EPA estimates that as many as one million asthmatic children have their condition worsened by exposure to ETS.

B. PUBLIC AND SCIENTIFIC REVIEWS OF THE EPA REPORT

A first external draft of this assessment was released for public review and comment in June 1990. In December 1990, EPA's Science Advisory Board (SAB), a committee of independent outside scientific experts in the field, conducted a review of the draft report and submitted its comments to the EPA Administrator in April 1991. In its comments, the SAB's Indoor Air Quality/Total Human Exposure Committee concurred with the primary findings of the report, but made a number of recommendations for strengthening it.

Incorporating recommendations from both the public and the SAB, a revised draft was transmitted to the SAB in May 1992 for a second review. Following a July 1992 public review meeting the

SAB panel endorsed the report and its conclusions, including a unanimous endorsement of the classification of environmental tobacco smoke as a Group A (known human) carcinogen.

The EPA also received and reviewed public comments on the second draft, and integrated all appropriate material into the final risk assessment. The final report was released in January 1993, at a joint press conference held by former Administrator Reilly and former Department of Health and Human Services Secretary Sullivan.

C. DIFFERENCES IN ANALYSIS, PROCESS, AND DOCUMENTATION BETWEEN THE EPA AND CRS REPORTS

As described above, the basis of EPA's conclusions on the human health effects of ETS is a total weight-of-evidence approach, which includes data on exposure, chemistry, animal and cell testing, as well as human studies on ETS, which provide the largest component. To support its findings that ETS is a "known human carcinogen", the EPA reviewed over 30 original studies on ETS and lung cancer, from eight different countries, and presented six major analyses of the dataset. The 530 page EPA report also presented over 100 original papers on the noncancer respiratory health effects of ETS. Together EPA's analyses of the human data alone on ETS health effects comprise well over 300 pages. This should be compared with the analysis in the CRS report which

1) references only 2 original papers on ETS and lung cancer and no original papers on the noncancer respiratory effects of ETS.

2) uses as its source material for critiquing the EPA report one position paper by the Tobacco Institute, and two papers published in Consumers' Research, a non-peer reviewed monthly magazine.

3) in a 5-page discussion on the health effects of ETS, primarily reiterates tobacco industry criticisms, most of which were aired at the open public reviews of the EPA report and were rejected by EPA's independent Science Advisory Board. There is no indication that the CRS conducted its own analysis of the evidence from the original sources.

4) is written by two economists, who by their own statement say, "Please note that we are trained as economists and our area of expertise relates to economic analysis and the associated areas of statistical inference and quantification of effects for purposes of cost-benefit analysis and related economic

policies. We do not have technical expertise in the physiological and biological transmission mechanisms of disease causing agents." (Statement of Dr. Jane G. Gravelle and Dr. Dennis Zimmerman, CRS, before The Subcommittee on Clean Air and Nuclear Regulation, Committee on Environment and Public Works, United States Senate, May 11, 1994)

5) has no stated peer review, compared with the EPA report, which was reviewed by a panel of 18 independent scientific experts in the field.

D. CRITIQUE OF THE CRS CRITICISMS OF THE EPA REPORT

Appendix A of the CRS Report (CRS-45 to CRS-49) contains several criticisms of EPA's report. These are responded to below.

1. The CRS report says that nonlinear relationships for health effects have been found for active smoking and cites page 44 of the Surgeon General's 1989 Report (CRS-45). This reference pertains to the British Physicians study (40,000 subjects) of active smoking and lung cancer. The CRS report ignores the dose-response relationship for lung cancer risk and number of cigarettes smoked per day from the much larger U.S. Veterans study (290,000 males) portrayed on the next page of the 1989 Surgeon General's Report, that suggests a linear relationship is quite reasonable. The data from another even larger U.S. study, the Cancer Prevention Study-I (previously American Cancer Society 25-State study; 840,000 subjects), are similarly consistent with a linear relationship, as are the data from many other studies of active smoking and lung cancer (See, for example, 1982 Surgeon General's Report, p.38). Furthermore, the CRS report does not cite any evidence for linear or nonlinear relationships for any health effects other than lung cancer.

2. The CRS report raises the question of how a passive smoking effect can be discerned from a group of 30 studies of which 6 are statistically significant (CRS-46 to CRS-47). This is an incomplete characterization of the total weight of evidence provided by these studies. For example, it overlooks the actual consistency of the study results. Twenty-four of the 30 studies found an increased risk of lung cancer in nonsmoking wives with smoking spouses compared to those with nonsmoking spouses. The fact that most did not achieve statistical significance is not surprising, because most of the studies had low statistical power to detect an effect, due to small sample sizes.

More importantly, these figures represent the data pertaining to an imprecise exposure measure--whether or not the spouse ever smoked. Spousal smoking is the most stable and sensitive single measure of ETS exposure; however, it is a crude measure because virtually everyone is exposed to ETS from a variety of sources. Therefore, women in the control group are not truly unexposed because they are exposed to ETS from sources other than spousal smoking. Furthermore, women in the exposed group are not all actually exposed to the largest relative exposures. Because of these "exposure misclassification" difficulties, the exposure differential between the control group and the exposed group is diluted, and the likelihood of being able to detect a relative effect is decreased.

To help overcome these difficulties it is important to look at what happens to the relative risks across exposure subgroups, for those studies that provide response data by exposure level, i.e. how much the spouse smoked. Comparing the high exposure groups to the control group provides a better exposure differential to determine whether or not there is an ETS effect. This is a standard practice in epidemiology. Seventeen of the 30 ETS and lung cancer studies provide information by exposure group; all 17 observed an increased risk in the highest exposure group. Nine of the 17 are statistically significant despite the further sample size reduction that occurs from subdividing the exposed group. Furthermore, all 14 studies that provide sufficient information for exposure-response trend tests show a positive exposure-response relationship, i.e. increasing risk with increasing exposure, and 10 of these are statistically significant.

The consistency of the results across the 30 studies, especially the high exposure group results and the dose-response relationships, provides compelling evidence that ETS is causally associated with lung cancer.

3. The CRS report implies that the EPA did something questionable in weighting the studies, "increasing the relative importance of studies with large sample size, studies that would tend to find more significant effects for passive smoking", and erroneously claims that the EPA "standardize[d] this diverse group of studies to account for statistically important differences in their methodologies" (CRS-47). In fact, the EPA, as one of its many analyses, combined the data for studies within countries. Studies between countries were not combined because of heterogeneity from country to country. Combining data from different studies provides an objective way to include data from both positive and nonpositive studies. The weighting procedure used, the inverse variance, is standard statistical

methodology. Furthermore, large studies are more likely to find statistically significant effects only if there is a true effect. If there were no association between ETS and lung cancer, the study size would be irrelevant.

4. The CRS points out that the EPA adjusted the results of each study for smoker misclassification bias (CRS-47). However, CRS did not clarify that smoker misclassification bias is the one known upward bias on the relative risk estimates, and that the adjustment has the effect of decreasing these estimates. The major source of bias, exposure misclassification, produces a downward bias on the relative risk estimates (see #2 above), and EPA did not adjust for this bias in making its carcinogenicity determination.

5. The CRS also emphasizes the fact that EPA used subjective judgments to "exclude" studies from its joint analysis (CRS-47). Again, the pooling of data was just one of the many analyses EPA conducted, and it was done both with and without tiering, which was based on explicit criteria. The results of the combined analysis, both with and without tiering, are consistent with the results of the analyses of the individual studies, and EPA's conclusion that ETS is a human lung carcinogen is not dependent on the combined analysis. Where a combined relative risk estimate is used for one of the quantitative analyses of the U.S. population risk, all of the U.S. studies are used.

6. The CRS says that the EPA changed "the standard for statistical significance from the usual standard, and the one generally used in the original studies" (CRS-47). The EPA used one-tailed 5% significance level tests to assess the results of the studies of ETS and lung cancer. This is a standard statistical technique when there is existing scientific evidence that, if there is an effect, it is likely to be in only one direction. Such is the case for lung cancer, because of the known carcinogenicity of active smoking and the chemical similarity between ETS and mainstream smoke. For the noncancer respiratory effects, where there was no such strong existing scientific evidence from active smoking, a two-tailed 5% significance level test was used. Furthermore, for the lung cancer studies, some of the original studies used one-tailed tests and some used two-tailed tests; when combining data, a single standard has to be used.

7. The CRS says that "the critical issue" is how large a chance we are willing to take that we accept the existence of a passive smoking effect when in fact one does not exist (CRS-48). The CRS description of the issue does not consider the consistency of the total evidence from the epidemiology studies (see #3), and the total weight-of-evidence as

described in Section A above. The 5% significance level used for the statistical testing reflects the probability of accepting an association from a single study when the association actually occurs by chance. The likelihood of the observed combination of results from the multiple studies of ETS and lung cancer occurring by chance is substantially lower. For example, the probability of 9 or more of 17 studies showing statistically significant associations for the highest exposure group by chance is less than 1-in-10-million. The probability of 10 or more of 14 studies showing statistically significant exposure-response relationships by chance is less than 1-in-a-billion.

8. The CRS report also suggests that different recollection of exposure by subjects with and without disease can bias the results (CRS-48). The results of the cohort studies, where exposure is ascertained before disease development, argues against such recall bias as being important in this case. Furthermore, the case-control study by Fontham et al,[1] used two different control groups, population controls and colon-cancer controls (who also have disease and, thus, may have different recall), to examine the issue of recall bias, and found no evidence of such bias.

9. The CRS report says that while EPA did make "some" adjustment for smoker misclassification, "it remains possible that a relationship observed might reflect the effects of active rather than passive smoking" (CRS-48). Again, the EPA did make an adjustment for smoker misclassification, and the procedure was specifically approved by the independent Science Advisory Board.

11. Similarly, the CRS acknowledges that the EPA "considered the presence of confounding factors in its evaluation of the studies", but says that "this issue is not laid to rest" (CRS-48). Hypothetical confounding is something that can never be fully ruled out; however, there is no evidence of such an effect for ETS and lung cancer. Several potential confounders were examined in the EPA risk assessment and were not found to affect the results. Furthermore, the epidemiology studies of lung cancer and ETS show consistent dose-response relationships in a variety of countries where diet and other lifestyle factors differ. There is no known factor that explains the consistent dose-response relationships observed in these diverse countries. For example, a high fat diet has been postulated as a

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[1] Fontham et al. (1991) Lung cancer in nonsmoking women: a multicenter case-control study. Cancer Epidemiol. Biomarkers Prev. 1:35-43.

confounding factor; however, the studies from Japan, where the diet is characteristically low in fat, show strong dose-response relationships for ETS and lung cancer. In addition, the study by Brownson et al. demonstrates lung cancer associations with both ETS[2] and dietary fat[3] in the highest exposure groups, yet finds no evidence that one factor confounds the other. The updated Fontham study[4] also examined a number of dietary and other potential confounders, and concluded that "the strong association in this study between adult ETS exposure and lung cancer risk cannot be attributed to any likely confounder"[4].

11. The CRS report says that two epidemiology studies that were published after the cutoff date for inclusion in the EPA report find no statistically significant increased lung cancer risk (CRS-48 to CRS-49). The CRS then says that both studies found a statistically significant increased risk in the highest exposure group, but that when large studies are "broken into several subsets and each is analyzed separately, some associations may be statistically significant by chance" (CRS-49). This comment does not reflect the consistency of the results for the highest exposure groups that the CRS notes two pages earlier (CRS-47). In addition, a third lung cancer study[5] that has come out since the EPA report, also showing an increased lung cancer risk in the highest exposure group. Including the 3 new studies and the update of the Fontham study[4], all 20 studies that provide data by exposure group find an increased lung cancer risk in the highest exposure group, and 13 of these are statistically significant, despite the small sample sizes.

12. The CRS report says that "many of the statistical concerns raised above with regard to lung cancer are relevant to respiratory effects in children" (CRS-49). However,

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[2] Brownson et al. (1992) Passive smoking and lung cancer in nonsmoking women. Am. J. Public Health 82:1525-1530.

[3] Alavanja et al. (1993) Saturated fat intake and lung cancer risk among nonsmoking women in Missouri. J. Natl. Cancer Inst. 85:1906-1916.

[4] Fontham et al. (1994) Environmental Tobacco Smoke and Lung Cancer in Nonsmoking Women: A Multicenter Study. JAMA 271:1752-1759.

[5] Liu et al. (1993) Indoor air pollution and lung cancer in Guangzhou, People's Republic of China. Am. J. Epidemiol. 137:145-154.

virtually none of the same concerns apply. i) The data on lower respiratory tract infections, for example, are even more consistent and show higher relative risk estimates than the lung cancer data. ii) Two-tailed significance tests were used for the noncancer effects. iii) Smoker misclassification is not an issue for infants and young children. iv) The noncancer studies were not pooled, so no issues of weighting or subjective tiering apply. v) Parental smoking is generally a very good surrogate of total ETS exposure in young children. vi) With acute effects, there is little concern for uncertain exposures in the distant past, so exposure recall is less of a problem. vii) Several noncancer studies[6] have biomarker evidence of ETS exposure, not just questionnaire data, and these biomarker data correlate with both the questionnaire data and the health effects, alleviating concerns about recall bias and about the validity of questionnaire data. viii) Studies that have come out since the EPA report are not just consistent with, but actually go further than, the EPA's conclusions pertaining to noncancer effects[7].

13. The CRS report raises the question of hypothetical confounding for the respiratory effects in children, saying that the "presence of other factors that may be related to these illnesses that are not controlled for are particularly important in the case of ... general respiratory illness, where the link between active smoking and disease is not as powerful as in the case of lung cancer" (CRS-49). The absence of a link between active smoking and respiratory effects in adults has little biological relevance to respiratory effects in children since young children represent a highly sensitive population because of their developing respiratory systems. As with lung cancer, the EPA did evaluate a number of potential confounding factors, and determined that they could not explain the observed associations. Furthermore, as with lung cancer, the consistent results observed across independent studies from

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[6] For example, Ehrlich et al. (1992) Childhood asthma and passive smoking: urinary cotinine as a biomarker of exposure. Am. Rev. Respir. Dis. 145:594-599; Etzel et al. (1992) Passive smoking and middle ear effusion among children in day care. Pediatrics 90:228-232; Reese et al. (1992) Relationship between urinary cotinine levels and diagnosis in children admitted to hospital. Am. Rev. Respi. Dis. 146:66-70; Chilmonczyk et al. (1993) Association between exposure to environmental tobacco smoke and exacerbations of asthma in children. N. Engl. J. Med. 328:1665-1669.

[7] Schoendorf and Kiely (1992) Relationship of sudden infant death syndrome on maternal smoking during and after pregnancy. Pediatrics 90:905-908.

a variety of countries, with different lifestyle factors, argue against confounding.

B. EPA COMMENTS ON THE HEALTH EFFECTS COMPONENTS OF THE CRS ASSESSMENT OF COSTS DUE TO PASSIVE SMOKING

Our comments relate only to the CRS's assumptions pertaining to the health effects of passive smoking, and do not address the economic basis for the CRS analysis.

The CRS derives cost estimates using three different methods, each of which raises concerns, which are detailed below:

1. "Estimate based upon EPA's estimate of deaths from lung cancer" (CRS-11 to 12). In this case, the CRS multiplies the total costs per pack from active smoking by the ratio of lung cancer deaths attributed to passive smoking divided by the number attributed to active smoking. On the one hand, this overestimates the costs per pack from passive smoking, because some of the active smoking costs do not apply to passive smoking, for example, the costs from fires and medical expenditures associated with emphysema. On the other hand, if the CRS is trying to estimate the costs for all health effects that may be associated with passive smoking, a different ratio should be used. For example, Steenland, in the same article cited by the CRS (CRS-12 and CRS-46), estimates that 35,000 to 40,000 heart disease deaths per year in nonsmokers are attributable to passive smoking[1]. Combining heart disease and lung cancer, which at least represent the two major causes of smoking-attributable mortality, yields a ratio of about 0.13[2], which is roughly six times higher than the ratio used by the CRS. Furthermore, the costs for respiratory effects in children from passive smoking should be added, because these are effects whose costs are not reflected in the total costs from active smoking.

2. "Estimate based upon EPA's estimate of child hospitalizations" (CRS-12). Here, the CRS estimates the costs of hospitalizations for children suffering from ETS-

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[1] Since the EPA has not assessed the role of ETS in heart disease, we are neither endorsing nor disavowing these estimates; we merely suggest that they be included for consistency in the CRS methodology.

[2] 37,500 heart disease deaths plus 3,000 lung cancer deaths per year attributable to passive smoking, divided by 313,000, the number of heart disease and lung cancer deaths attributed to active smoking in 1988 [MMWR (1991) 40(4):63].

attributable lower respiratory tract infections. Other costs for respiratory effects in children resulting from passive smoking should be included, for example, hospitalizations for asthma attacks and for middle ear effusion, as well as costs of doctor visits and treatments for cases of lower respiratory tract infections, asthma, and middle ear effusion not requiring hospitalization.

3. "Estimate based upon relative physical exposure to smoke" (CRS-12). This method involves multiplying "the estimate of total active-smoking costs by the ratio of nonsmokers-to-smokers' physical exposure to smoke and by the ratio of nonsmoker to smokers" (CRS-12). The EPA believes that estimates of passive smoking effects based on "physical exposure to smoke" extrapolated from active smoking to passive smoking, rather than on the epidemiology data for passive smoking, are erroneous. There is no scientifically valid ratio of "physical exposure to smoke" between active and passive smokers. The CRS uses the ratio of urinary cotinine, but cotinine is a metabolite of nicotine, which is just one of over 4,000 compounds in tobacco smoke. Different compounds yield different ratios and are associated with different health effects. Nicotine, in particular, is known to underestimate exposures to many other ETS toxicants, because it adheres readily to materials in indoor environments and is therefore more rapidly removed from contaminated air than are other constituents. Thus, nicotine is similarly likely to underestimate health risks when extrapolating from active to passive smoking.

After adjusting for the "higher total active-smoking costs" estimated in the Manning study, the CRS states that its passive smoking cost estimates "seem rather high" and attempts to discount them (CRS-13). First, it states that "the epidemiological evidence for passive-smoking-related disease is weak" (CRS-13). The EPA strongly disagrees with this statement as noted above (See Sections A-D). Second, the CRS states that "the estimates based upon physical exposure assume a linear relationship between exposure and disease" and that nonlinear relationships for health effects have been found with respect to active smoking. As noted in #3 above, the EPA believes that the estimates based on physical exposure are unreliable because the concept of extrapolating "physical exposure to smoke" is flawed. Furthermore, as stated in #1 of Section D, the EPA disagrees with the statement that the relationships between exposure and health effects are "strongly nonlinear". The CRS cites as its basis page 44 of the Surgeon General's 1989 Report (CRS-13). This reference pertains to one British study of active smoking and lung cancer. The CRS report cites no evidence for nonlinear dose-response relationships for any other health effects and does not address data from the many other studies of lung cancer and

active smoking, including data from a much larger U.S. study that appear on the next page of the Surgeon General's Report, that suggest a linear relationship is reasonable.

attributable lower respiratory tract infections. Other costs for respiratory effects in children resulting from passive smoking should be included, for example, hospitalizations for asthma attacks and for middle ear effusion, as well as costs of doctor visits and treatments for cases of lower respiratory tract infections, asthma, and middle ear effusion not requiring hospitalization.

3. "Estimate based upon relative physical exposure to smoke" (CRS-12). This method involves multiplying "the estimate of total active-smoking costs by the ratio of nonsmokers-to-smokers' physical exposure to smoke and by the ratio of nonsmoker to smokers" (CRS-12). The EPA believes that estimates of passive smoking effects based on "physical exposure to smoke" extrapolated from active smoking to passive smoking, rather than on the epidemiology data for passive smoking, are erroneous. There is no scientifically valid ratio of "physical exposure to smoke" between active and passive smokers. The CRS uses the ratio of urinary cotinine, but cotinine is a metabolite of nicotine, which is just one of over 4,000 compounds in tobacco smoke. Different compounds yield different ratios and are associated with different health effects. Nicotine, in particular, is known to underestimate exposures to many other ETS toxicants, because it adheres readily to materials in indoor environments and is therefore more rapidly removed from contaminated air than are other constituents. Thus, nicotine is similarly likely to underestimate health risks when extrapolating from active to passive smoking.

After adjusting for the "higher total active-smoking costs" estimated in the Manning study, the CRS states that its passive smoking cost estimates "seem rather high" and attempts to discount them (CRS-13). First, it states that "the epidemiological evidence for passive-smoking-related disease is weak" (CRS-13). The EPA strongly disagrees with this statement as noted above (See Sections A-D). Second, the CRS states that "the estimates based upon physical exposure assume a linear relationship between exposure and disease" and that nonlinear relationships for health effects have been found with respect to active smoking. As noted in #3 above, the EPA believes that the estimates based on physical exposure are unreliable because the concept of extrapolating "physical exposure to smoke" is flawed. Furthermore, as stated in #1 of Section D, the EPA disagrees with the statement that the relationships between exposure and health effects are "strongly nonlinear". The CRS cites as its basis page 44 of the Surgeon General's 1989 Report (CRS-13). This reference pertains to one British study of active smoking and lung cancer. The CRS report cites no evidence for nonlinear dose-response relationships for any other health effects and does not address data from the many other studies of lung cancer and

active smoking, including data from a much larger U.S. study that appear on the next page of the Surgeon General's Report, that suggest a linear relationship is reasonable.